Docket No.: SMI-005.01
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Isa Odidi *et al.*

Application No.: 09/166,701 | Confirmation No.: 9432

Filed: October 5, 1998 | Art Unit: 1614

For: CONTROLLED RELEASE PHARMACEUTICAL DELIVERY DEVICE AND PROCESS FOR PREPARATION THEREOF | Examiner: S. V. Gembeh

DECLARATION UNDER 37 C.F.R. § 1.132

1. Isa Odidi and Amina Odidi hereby declare as follows:

2. We are co-inventors of and are familiar with the present U.S. Patent Application Serial No. 09/166,701 ("the '701 application"), including the presently pending claims, and we are familiar with the Office Action mailed on November 13, 2008 ("the Office Action"), in the present application.

3. We have also reviewed the documents cited by the Examiner in the Office Action, namely U.S. Patent No. 4,252,786 to Weiss et al. ("Weiss") and U.S. Patent No. 4,940,587 to Jenkins et al. ("Jenkins").

4. Weiss describes a two-step process to make a controlled release dosage form containing two compartments. The first is an inner compartment made of a matrix core containing the drug and the second is an outer coating made of a polymer film coat comprising a combination of polymers to modify the drug release rate. Thus, the Weiss tablets are compartmentalized. They have an inner core comprising the drug and outer core comprising a polymer film coat.

5. The present claims, in contrast to Weiss, are directed to a controlled release pharmaceutical composition, wherein all of the recited components, including the drug, are provided as a homogenous mixture.

6. We have conducted experiments to establish that the release rate profile of the presently claimed composition is different from the release rate and profile of the composition described by Weiss. As discussed below, two formulations of controlled release Metformin HCl where made: one according to the present application and the other according to Weiss.

7. Table 1 shows a formula according to the present application, notably 20% of hydroxyethyl cellulose and 35% of hydroxypropylmethyl cellulose were homogenously blended with carbovinyl polymer (Carbopol), metformin HCl and the other excipients to form a homogenous blend. The homogenous blend was compressed to form tablets of 200 mg weight.

8. A formula according to Weiss et al's teachings are shown in Tables 2 and 3. Table 2 shows content of the inner matrix tablet, while Table 3 shows content of the outer ruptureable coat. Tablets weighing 90mg were made out of the inner matrix tablet mixture. These contained 20 mg Metformin HCl, but did not contain hydroxyethyl cellulose and hydroxypropylmethyl cellulose. Following Weiss et al's teachings, the 90 mg tablets were then coated with hydroxyethyl cellulose and hydroxypropylmethyl cellulose to bring the total weight per tablet to 200 mg.

9. Thus, the tablets according to the present invention and those according to the teaching of Weiss et al, contain the same type of ingredients in the same amounts, except that in the case of the Weiss et al tablets, hydroxyethyl cellulose and hydroxypropylmethyl cellulose are not in a homogenous blend with the rest of the materials that make up the Weiss tablets, ie., they are in a separate compartment.

10. Table 4 and Figure 1 show the dissolution of each of the above examples over a 13 hour period of time. The Weiss tablet releases the drug in a two step process, i.e., there is a lag phase of nearly 1 hour before the drug begins to be released from the tablet, followed by a faster rate of drug release (a dual drug release mechanism). Thus, the function of the outer coat seems to be that of slowing initial phase of drug release.

11. On the contrary, the present application approach surprisingly results in drug being released in a one step process in which drug is released over time without a lag phase (see Figure 1). Table 5 and Figure 2 show results from an example of the teaching of Weiss et al taken from US Patent 4,252,786 (Weiss). These results are in agreement with the above discussions.

12. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code and that willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Isa Odidi

Dated: 11 May 2009 Signature: _____

Amina Odidi

Dated: May 11, 2009 Signature: _____

Appendix

Table 1.
Formula for tablets made from a Homogenous blend in accordance with the '701 application.

Materials	**%**	**g/ 1000g batch**	**g/ 5000g batch**
Metformin HCl	10	100	500
Lactose	19.5	195	975
Hydroxypropyl methyl cellulose	35	350	1750
Hydroxyethyl cellulose	20	200	1000
Cabopol	7	70	350
MCC	8	80	400
Magnesium Stearate	0.5	5	25
Grand Total	**100**	**1000**	**5000**

Formulation prepared according Weiss et al US Patent #: 4252786

Table 2
I. Formula for the inner Matrix tablet Core

Materials	%	g/ 1000g batch	g/ 5000g batch
Metformin HCl	22.22	100	500
Lactose	43.33	195	975
Hydroxypropyl methyl cellulose	0	0	0
Hydroxyethyl cellulose	0	0	0
Cabopol	15.56	70	350
MCC	17.78	80	400
Magnesium Stearate	1.11	5	25
Total	100	450	2250

Matrix tablet core each weighing 90mg was made according to Weiss et al, US Patent #: 4252786

Table 3
II. Formula for the outer rupturable film coat

Materials	%	g/ 1000g batch	g/ 5000g batch
Hydroxypropyl methyl cellulose	63.64	350	1750
Hydroxyethyl cellulose	36.36	200	1000
Ethyl alcohol	Quantity sufficient	Quantity sufficient	Quantity sufficient
Total	100	550	2750
Grand Total		**1000**	**5000**

Sufficient to coat the inner matrix tablet core to a final weight of 200mg

Table 4
Comparative dissolution for Metformin hydrochloride controlled release tablets made according to the present application and those made according to Weiss.

Time[hr]	Metformin made according to US Patent App. No. 09/166701 (Odidi) (%)	Metformin made according to US Patent #: 4252786 (Weiss) (%)
0	0	0
1	43	7
2	60	59
3	71	84
4	78	94
5	83	98
6	87	102
7	89	105
8	91	105
9	92	105
10	93	105
11	94	105
12	94	105
13	96	105

Figure 1

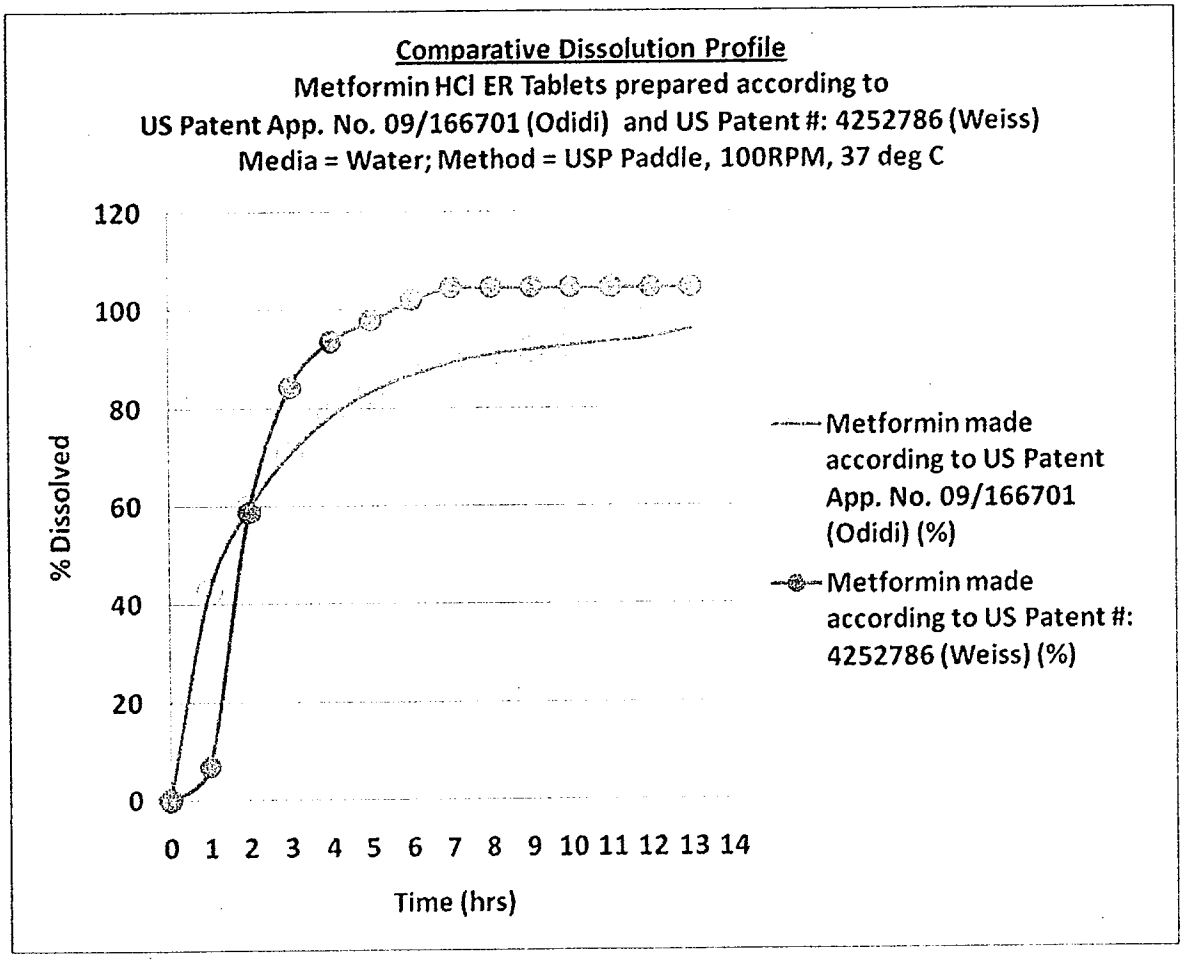
Comparative Dissolution Profile
Metformin HCl ER Tablets prepared according to
US Patent App. No. 09/166701 (Odidi) and US Patent #: 4252786 (Weiss)
Media = Water; Method = USP Paddle, 100RPM, 37 deg C
% Dissolved
120
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Time (hrs)
Metformin made according to US Patent App. No. 09/166701 (Odidi) (%)
Metformin made according to US Patent #: 4252786 (Weiss) (%)

Table 5

Comparative dissolution at different time intervals for Procainamide hydrochloride controlled release dosage example taken from US Patent #: 4252786 (Weiss)

Time Hrs	Coated from Weiss (% Procainamide)	Uncoated from Weiss (% Procainamide)
0	0	0
1	14.6	40
2	34.7	51.8
3	48	66.2
4	68	76
5	83	79.6
6	89.3	82.8
7	95	85.8
8	97.1	85.8
10	107	91.2

Figure 2